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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/803,319	ANDERSON ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-58* is/are pending in the application.

4a) Of the above claim(s) *7,12-14,21-56 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 6, 8-11, 15-20 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3 and 5-58 are pending. Claims 7, 12-14, 21-56 and 58 are withdrawn from consideration. Claims 1-3, 5, 6, 8-11, 15-20 and 57 are examined.

2. The examiner respectfully notes that claims 1 and 2, as amended in the paper entered 6/19/2006, now recite the added limitation that the cytophobic surface comprises a hydrogel; that canceled claim 4 recited this same limitation that the cytophobic surface comprises a hydrogel; and that now canceled claim 4 previously was rejected over maintained prior art under 35 U.S.C. §§ 102 and 103, (see below).

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/19/2006 has been entered.

Election/Restrictions

4. The Requirement for Restriction/Election, mailed 7/10/2002 is maintained, as well as applicant's election, filed 7/18/2002, of Group I (originally claims 1-20) and

species (non covalent, chemical adsorption; glass; homopolymers of methacrylic esters, poly(2-hydroxy-ethylmethacrylate); further comprising a compound, a non-covalently bound drug; and synthetic polymers, polyhydroxyacids). The elections were treated as without traverse in the Office action mailed 10/28/2002. Upon consideration, claim 14 was withdrawn as drawn to an unelected species in the Office action, mailed 2/18/2005.

Claims 21-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Inventions, there being no allowable generic or linking claim (see, e.g., previous Office action, mailed 9/7/2004).

Claims 7, 12-14, 55, 56, 58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/18/2002.

5. In regard to the Requirement for Restriction/Election, mailed 7/1/2002, the examiner notes that a restriction between was required between Inventions drawn to a microarray, methods for using the microarray, and methods of making the microarray.

> The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.
>
> In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined

process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

6. The instant application was filed 3/9/2001.

Maintained Claim Rejections - 35 USC § 102

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 1-3, 5, 8-11 and 15-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kim et al., US 6,699,665. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-

covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers.

Kim et al., throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, or proteins libraries. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Response to Arguments

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

Response to Arguments

Applicant's argues that the Declaration filed under 37 CFR 1.131, which was not considered sufficient by the examiner, as set forth in the previous Office action, is, in

fact sufficient; and applicant argues that the arguments and claim amendments overcome all rejections and render any disagreement about the Declaration moot.

Applicant argues that polymethylacrylate, as disclosed by Kim, is not a hydrogel, as recited in amended claims 1 and 2. Applicant argues that the Kim reference, in fact, provides evidence that polymethylacrylate is not a hydrogel, because Kim at col. 11, lines 23-24, describes polystyrene, poly(methyl methacrylate) and polycarbonate as "rigid materials". Applicant argues that Kim's disclosure indicates that a rigid material should be employed as a substrate in contrast to amended claims 1 and 2.

Applicant's arguments, entered 6/19/2006, have been fully considered but they are not persuasive.

The examiner respectfully maintains the position that the Declaration filed under 37 CFR 1.131, is not sufficient to overcome the prior art references, for the reasons as set forth in the prior Office action. The examiner respectfully disagrees that the arguments and amendments, entered 6/19/2006, place the application in condition for allowance.

The examiner respectfully notes that the instant specification, at p. 6, lines 9-23, especially lines 15 and 19-20, discloses that poly(methacrylic acid ester), including poly(methyl methacrylate), are hydrogels. The examiner respectfully submits that because the poly(methyl methacrylate) of the instant specification is a hydrogel, the poly(methyl methacrylate), as taught by Kim, is a hydrogel. Furthermore, the instant

specification does not provide a limiting definition of hydrogels and does not address rigidity of substrates.

Furthermore, Kim et al., at Example 2, col. 14, line 64-col. 15, line 22, especially col. 15, lines 9-10, teach arrays comprising the elected species, polyhydroxy ethyl methacrylate, wherein said polyhydroxy ethyl methacrylate is a hydrogel.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., rigid materials not used as substrates, as in claims 1 and 2) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Instant claims 1 and 2 are silent in regard to "rigid" materials.

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness."). MPEP 2145. Applicant's representative suggests that "rigid materials", such as polystyrene, poly(methyl methacrylate) and polycarbonate, cannot be hydrogels. The examiner respectfully submits that this is mere arguments of counsel, and that applicant do not provide objective evidence that this is a true fact.

It is respectfully noted that now canceled claim 4, which claimed hydrogels, was rejected over the instant aforementioned prior art reference(s) in previous Office actions.

New Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1, 2, 3, 5, 8-11, and 57 are rejected under 35 U.S.C. 102(e) as being anticipated by Lewis et al., US 6,290,911 B1.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, the cytophobic surface comprising a hydrogel; and a plurality of discrete dry (non-monolayer) polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers; and variations thereof.

Lewis et al., throughout the patent, and abstract, and at col. 3, lines 40-50, teach first and second organic materials that are combined, for example by surface interpenetration, reading on non-covalent, non-monolayer binding, to form sensors, said sensors forming arrays or grids, (Lewis at col. 10, line 49-col. 11, line 5) reading on a microarray of polymeric biomaterials, as in instant claims 1 and 2. Lewis et al., at col. 9, lines 59-col. 10, line 21, teach an array wherein a first organic material in solution ("x") is contacted with a region, and then contacted with a second organic material ("y") in solution, reading on different soluble synthetic polymers, as in the claims. See, Lewis et al., at col. 7, lines 23-42, col. 10, lines 9-12. Lewis et al. col. 8, lines 13-46, teach a variety of organic polymers, including poly(methacrylics) and poly(methacrylate), reading on a base comprising a cytophobic surface, the cytophobic surface inherently comprising a hydrogel. The examiner respectfully notes that the instant specification, at p. 6, lines 9-23, especially lines 15 and 19-20, discloses that poly(methacrylic acid ester), including poly(methyl methacrylate), are hydrogels. In Example 1, Lewis at col. 17-20, teaches two organic polymers, that are placed onto a glass slide, reading on the glass base of claim 3.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by

process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Lewis et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

Maintained Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1-3, 5, 6, 8-11, 15-20, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Schultz et al., US 5,985,356**, (IDS filed 3/11/2003); **Sheu et al.**, (J. Adhesion Sci. Technol., 1992, Vol. 6, No. 9, pp. 995-1009); **Kapur et al., US 6,548,263**, (previously cited by examiner, 11/21/2003); and **Koob et al., US 20030204023**. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Schultz et al. (US 5,985,356), throughout the patent, teach microarrays of polymeric biomaterials comprising: a base (including metals and glass) comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements that include polyurethanes, polycarbonates, polystyrene, (col. 7, lines 34-56; col. 11, line 41-col. 12, line 5; and as in instant claim 11) non-covalently bound to said surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers. Schultz et al., at col. 4, lines 30-46, teach that an array of materials on a single substrate can consist of more that 10, more than 100, more than 1000 materials, and so fourth. Schultz et al. at col. 33, lines 14-51, and Figure 9, teach synthesis of an array of 16 different organic polymers of styrene and

acrylonitrile and initiator, wherein the monomers are delivered by ink-jet dispenser; upon completion of polymerization on the substrate, the organic solvent is removed by evaporation *in vacuo*, which reads upon dry polymeric biomaterial elements. Schultz et al., at col. 11, line 41-col. 12, line 5, teach arrays of diverse materials at known locations on a single substrate surface and teach that the substrates can be coated with a material different from the base, and state that "[t]he most appropriate substrate and substrate-surface materials will depend on the class of materials to be synthesized and the selection in any given case will be readily apparent to those of skill in the art." Schultz et al., at col. 15, lines 18-65, also teach thin-film deposition techniques. Schultz et al. at col. 12, lines 6-34, teach regions that are less than 1,000 μm^2 (as in claims 15 and 16). Schultz et al., at col. 23, lines 35-48, disclose that spacing between the individual regions will vary in accordance with the sized of the regions used, for example, if a 1 mm^2 region is used, the spacing will be on the order of 1 m or less. If a 10 μm^2 region is used, then the spacing will be on the order of 10 μm. Thus the intervals as claimed in claims 17 and 18 are within the ranges taught by Schultz et al. At col. 4, lines 30-47, Schultz et al. teach 1 to 10 to 100 to 1000 to 10,000 regions/cm^2, so that if one compound is polymerized on one region, then the density of polymeric biomaterial elements per cm^2 is encompasses the ranges claimed in claims 19 and 20.

Schultz et al. (US 5,985,356), does not disclose microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, wherein polymeric elements are bound to the cytophobic surface; and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug. Schultz et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Sheu et al., (J. Adhesion Sci. Technol., 1992, Vol. 6, No. 9, pp. 995-1009), throughout the publication and especially in the abstract, p. 995, para 1-p. 996, para 1, teach non-fouling surfaces, including surfaces containing poly(ethylene glycol) (PEG) or poly(ethylene oxide) (PEO) that show high surface wettability and low affinity for proteins and cells. Sheu et al., at p. 998, teach dip-coating surfaces to deposit PEO surfactants.

Kapur et al., (US 6,548,263), throughout the patent, and especially at col. 41, line 43-col. 43, line 6, teach arrays of various sizes, rendering array surfaces repulsive for cellular adhesion, in order to pattern cell attachment and growth on a surface; and Kapur et al. teach using hydrogel as a cytophobic surface. Kapur et al., at, e.g., col. 18, line 60-col. 19, line 65, especially col. 19, line 48, teach that various cell binding, marker and other molecules can be used in the arrays, including "drugs".

Koob et al., US 20030204023, at para [0155] teach that poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and polymeric elements that are bound to the cytophobic surface; wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate); and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and wherein polymeric elements are bound to the cytophobic surface, in order to avoid following of substrates by protein and cells and to control the patterns of cell growth on substrates. Schultz et al. teach that the practitioner may select a substrate upon which to generate a polymeric array, depending upon the material to be synthesized; Sheu et al., teach that the synthesis of cytophobic surfaces coated with PEG or PEO so as to prevent fouling by proteins and cells; and Kapur et al. using multiple layers of cell adhesive and cell repulsive surfaces to control the pattern of cell growth on surface. One of ordinary skill in the art would have been motivated to make cytophobic surface that comprises poly(2-hydroxy-ethyl methacrylate) because Koob et al. teach poly(2-hydroxy-ethyl methacrylate) is cytophobic.

One of ordinary skill in the art would have had a reasonable expectation of success in combining the teachings of Schultz et al., Sheu et al., and Kapur et al., because Sheu et al. and Koob et al. taught cytophobic surfaces, including poly(2-hydroxy-ethyl methacrylate), were well known in the art at the time the invention was made; and because polymerization on substrates is taught by Schultz et al.

Response to Arguments

Applicant argues that the combination of the aforementioned prior art references would result in the disclosure of Kapur, in which cytophobic and cytophilic material are deposited side-by-side on a substrate, and not the invention recited in claims 1 and 2.

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface, and wherein polymeric elements are bound to the cytophobic surface, in order to avoid following of substrates by protein and cells and to control the patterns of cell growth on substrates. Schultz et al. teach that the practitioner may select a substrate upon which to generate a polymeric array, depending upon the material to be synthesized; Sheu et al., teach that the synthesis of cytophobic surfaces coated with PEG or PEO so as to prevent fouling by proteins and cells; and Kapur et al. using multiple layers of cell adhesive and cell repulsive surfaces to control the pattern of cell growth on surface.

Response to Arguments

Applicant argues that Schultz et al. fails to disclose a cytophobic surface comprising a hydrogel, as recited in amended claims 1 and 2. Applicant argues that none of Sheu, Kapur and Koob remedy the failure of Schultz to disclose the claimed invention. Applicant argues that Sheu does not disclose a hydrogel. Applicant argues that Kapur fails to disclose a hydrogel. Applicant argues that Koob fails to disclose an array or the binding of a polymeric element to a cytophobic surface. Applicant argues that Koob is the only one of the references cited in the rejection "to even suggest the use of a hydrogel in any manner (paragraph 0089), and that one of the cited references teach or suggest how to deposit a hydrogel onto a substrate or how to deposit a polymeric biomaterial element onto a hydrogel, as recited in the claims". Reply at p. 12.

Applicant's arguments, entered 6/19/2006, have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

The reference of Koob et al., contrary to applicant's arguments, and as stated in the previous Office actions, teaches the use of hydrogels as a cell repulsive compound, e.g., in Example 4, col. 44, line 8, and in Example 5, col. 51, line 63.

Applicant admits that Koob discloses the use of a hydrogel, but argues that none of the references teach how to deposit a hydrogel onto a substrate or how to deposit a polymeric biomaterial element onto a hydrogel, as recited in the claims. However, Schultz et al., at col. 11, lines 42-44, discloses methods of preparing an array of "diverse materials at known locations on a single substrate surface." The prior art reference of Schultz, at col. 11, lines 44-45, states that "[e]ssentially, any conceivable substrate can be employed in the invention." Shultz et al., at col. 11, lines 46-49, states that these substrates can be organic, inorganic, biological, nonbiological, or *a combination of these*, which can exist as, among other forms, as *gels*, sheets and films. Schultz et al., throughout the patent, and e.g., at col. 4, lines 1-17, teaches methods of deposition onto a substrate.

Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "how to deposit a hydrogel onto a substrate or how to deposit a

polymeric biomaterial element onto a hydrogel") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The examiner therefore, respectfully submits that the prior art teaches the use of hydrogels as cytophobic substrates, that several of the references specifically teach hydrogel substrates as cytophobic, and that the references, taken as a whole, and in combination together, teach the claimed invention, as amended.

It is respectfully noted that now canceled claim 4, claiming hydrogels, was rejected over the instant aforementioned prior art reference(s) in previous Office actions.

13. Claims 1-3, 5, **6**, 8-11, and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kim et al., US 6,699,665**; and **Koob et al., US 20030204023**. This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Kim et al., US 6,699,665, throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic

and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, peptides, polypeptide, or oligopeptides. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Kim et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

Koob et al., US 20030204023, at para [0155] teach that poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate) because Koob et al., teach poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using cytophobic surfaces that comprise poly(2-hydroxy-ethyl methacrylate) because poly(2-hydroxy-ethyl methacrylate) is a hydrogel.

Response to Arguments

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

Response to Arguments

Applicant argues Koob fails to remedy the failure of Kim to teach a polymeric biomaterial element deposited on a hydrogel.

Applicant's arguments, entered 6/19/2006, have been fully considered but they are not persuasive. The examiner respectfully submits that the reference of Kim et al. does disclose and suggest polymeric biomaterial elements deposited on a hydrogel, (see above rejection of claims 1-3, 5, 8-11 and 15-20 under 35 U.S.C. 102(e) as being anticipated by Kim et al., US 6,699,665).

The examiner notes, parenthetically, that while Kim et al. teach polyhydroxy ethyl methacrylate, Kim et al. does not appear to explicitly disclose poly(2-hydroxy-ethyl methacrylate).

It is respectfully noted that now canceled claim 4, claiming hydrogels, was rejected over the instant aforementioned prior art reference(s) in previous Office actions.

14. Claims 1-3, 5, 8-11 and 15-20 and **57** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kim et al., US 6,699,665**; and **Kapur et al., US 6,548,263**, (previously cited by examiner, 11/21/2003). This rejection is maintained for the reasons of record as set forth in the previous Office action. The rejection is copied below for the convenience of the reader.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, and a plurality of discrete dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements

includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

Kim et al., US 6,699,665, throughout the patent and especially at col. 4, line 58-col. 5, line 38, teach a microarray of polymeric biomaterials comprising a base (including metal, glass, polystyrene, and polycarbonate), and teach a cytophobic surface, wherein the base is polymethylacrylate, which absent evidence to the contrary, is a hydrogel, as in claim 5, (specification at col. 6, lines 24-49); and an array of biomolecules that include molecules having a specific reactivity toward a particular surface, the remainder of the molecule being typically a hydrocarbon chain, which can be hydrophobic, cytophobic, or biophobic and is generated onto an substrate as a self-assembled monolayer (col. 9, lines 4-40) by direct coupling or by micro-contact printing; and, at col. 15, lines 45-67, teach an array of biomolecules prepared from solution of proteins ("e.g., 100 different proteins from a library) using an ink-jet; and at col. 8, lines 3-23, teach reactions (including ionic interaction, binding events, hydrophobic interaction, hydrogen bond formation, etc.) of the biomolecules, (including proteins, nucleic acids or chemical entities) with a substrate (which reads on a plurality of discrete, dry non-monolayer polymeric biomaterial elements non-covalently bound to said cytophobic surface), wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as claimed). Kim et al. at col. 7, lines 29-33, teach polymeric biomaterial elements ranging from 1 micron to about 1 mm, (as in claims 15 and 16); and at col. 7, lines 13-18, teach intervals measuring 1 cm to about 0.5 cm to about 0.25 cm distances, (as in claims 17 and 18). Kim at col. 10, lines 19-28, teach over 2,000 array elements in the area of a standard well of a 96-well plate (approximately mm^2), which absent evidence to the contrary, read on claims 19 and 20, reciting limitation of 1 to 1000 or 10-100 polymeric biomaterial elements per cm^2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements. Thus the microarrays taught by Kim et al., absent evidence to the contrary, do not differ in a structural or otherwise meaningful way from the microarrays of the claimed invention.

In regards to the limitation that the polymeric biomaterial elements include different soluble synthetic polymers, it is note that the specification does not disclose how synthetic polymers of poly(amino acids) differ from proteins, peptides, polypeptide, or oligopeptides. Absent evidence to the contrary, the proteins and protein libraries as taught by Kim et al. do not differ from synthetic polymers of poly(amino acids).

Kim et al. do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

Kapur et al., US 6,548,263, at, e.g., col. 18, line 60-col. 19, line 65, especially col. 19, line 48, teach that various cell binding, marker and other molecules can be used in the arrays, including "drugs".

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug.

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface and wherein at least one of said polymeric biomaterial elements further comprise a small molecule drug, because Kapur et al., teach testing and interacting cells with small drug molecules on arrays.

One of ordinary skill in the art would have had a reasonable expectation of success in making arrays that comprised small drug molecules, because the attachment of small organic molecules to polymers was well known in the art.

Response to Arguments

Applicant argues that in view of the Declaration under 37 CFR 1.131, the reference of Kim et al. does not qualify as prior art under 35 USC 102(e).

Applicant's arguments entered 8/22/2005 have been fully considered but they are not persuasive. The examiner respectfully submits that the Declaration is insufficient, (see above section Declaration Under 37 CFR 1.131).

Response to Arguments

Applicant argues Kapur fails to remedy the failure of Kim to teach a polymeric biomaterial element deposited on a hydrogel.

Applicant's arguments, entered 6/19/2006, have been fully considered but they are not persuasive. The examiner respectfully submits that the reference of Kim et al. does disclose and suggest polymeric biomaterial elements deposited on a hydrogel, (see above rejection of claims 1-3, 5, 8-11 and 15-20 under 35 U.S.C. 102(e) as being anticipated by Kim et al., US 6,699,665).

New Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1, 2, 3, 5, **6**, 8-11, and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Lewis et al., US 6,290,911 B1**; and in view of **Koob et al., US 20030204023**, (of record).

Lewis et al., US 6,290,911 B1 is relied upon, as in the above rejection under 35 U.S.C. 102(e).

Lewis et al., do not disclose a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface and wherein the cytophobic surface comprises specifically comprises poly(2-hydroxy-ethyl methacrylate).

Koob et al., US 20030204023, at para [0155] teach that poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate).

One of ordinary skill in the art would have been motivated to have made microarrays of polymeric biomaterials comprising a base comprising a cytophobic

surface and wherein the cytophobic surface comprises poly(2-hydroxy-ethyl methacrylate) because Koob et al., teach poly(2-hydroxy-ethyl methacrylate) is a cell attachment inhibitor.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using cytophobic surfaces that comprise poly(2-hydroxy-ethyl methacrylate) because poly(2-hydroxy-ethyl methacrylate) is a hydrogel.

Double Patenting

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 1-3, 5, 6, 8-11, 17, 18, and 57 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 41,

43, 50, 51, 52, 57, 58, 59, 62, 66, 67, 81 of **copending Application No. 10/214,723**. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims are drawn to a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, the cytophobic surface comprising a hydrogel; and a plurality of discrete dry (non-monolayer) polymeric biomaterial elements non-covalently bound to said cytophobic surface, wherein each of said polymeric biomaterial elements includes a soluble synthetic polymer, and at least two of said polymeric biomaterial elements include different soluble synthetic polymers; and variations thereof.

The product claims of the '723 Application are product of process claims that are drawn to a microarray of polymers comprising a plurality of discrete polymer elements bound to a surface ('723 Application at claim 41), wherein the surface of the microarray is cytophobic ('723 Application at claim 51), wherein the surface is a hydrogel ('723 Application at claim 52), reading on a microarray of polymeric biomaterials comprising: a base comprising a cytophobic surface, the cytophobic surface comprising a hydrogel and a plurality of discrete polymeric biomaterial elements, as in instant claims 1 and 2. Claim 41 of the '723 Application claims an array wherein the discrete polymer elements are bound to the surface by surface interpenetration, reading on polymeric biomaterials non-covalently bound to the surface, as in instant claims 1, 2, 8 and 9. Claim 41 of the '723 Application is drawn to providing solutions of monomers of polymer material, reading on soluble synthetic polymer, as in instant claims 1 and 2. Claims 43, 58, 62,

81 of the '723 Application recites a variety of monomers, (and as in instant claims 5, 6, 10, 11) thereby making obvious, in a product by process claim, polymeric biomaterial wherein at least two of said polymeric biomaterial elements include different soluble synthetic polymers, as in instant claims 1 and 2.

In regards to the limitation that the microarray be comprised of dry polymeric biomaterial elements, it is noted that in the examples of the instant application, microarrays with dry polymeric elements are placed into (cell) medium, so that at the time of use, the polymeric elements are not taught in the instant specification as dry. As it does not appear to be structurally necessary that the microarray be composed of dry polymeric elements in order to function, it appears that the claims are product by process claims. Furthermore, the instant specification does not teach that dry polymeric elements have structural limitations not found in wet polymeric elements.

Claim 50 of the '723 Application recites a surface comprising various materials, such as glass, polymer, metal, ceramic, as in instant claim 3. Claim 59 of the '723 Application claims a microarray comprising drugs, as in instant claim 57. Claims 66 and 67 are drawn to microarrays wherein the polymer elements are spaced at intervals between 300 micrometers, or less, and about 1200 micrometers, making obvious instant claims 17 and 18.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

19. Claims 1-3, 5, 6, 8-11, 15-20 and 57 are rejected. Claims 7, 12-14, 21-56 and 58 remain withdrawn from consideration.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark L. Shibuya
Examiner
Art Unit 1639